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REWARD

Restraint from risky reward

> “light stimulation of shock-responsive mPFC→NAc neurons (but not stimulation of all mPFC→NAc neurons) during the 5 s tone suppressed lever pressing”

The ability to suppress reward-seeking behaviour in the face of risk of punishment is adaptive. Previous research has implicated the medial prefrontal cortex (mPFC) in the inhibition of reward seeking, but the precise mPFC projections that are responsible remain unclear. Now, Kim *et al.* identify projections from the mPFC to the nucleus accumbens (mPFC→NAc projections) that suppress reward-seeking behaviour.

mPFC neurons project to several parts of the reward circuitry, including the NAc. To determine the possible importance of this population in reward seeking, the authors trained mice to press a lever to obtain a reward, and recorded the calcium responses of these cells on ‘baseline’ days (when a lever press led only to a reward) and on ‘shock’ days (when 30% of lever presses led to the animal being foot-shocked). The activity of mPFC→NAc neurons decreased and increased on receipt of a reward or shock, respectively. Notably, the activity of mPFC→NAc neurons dropped just before initiation of a complete lever press on shock days, but not on baseline days, suggesting that maintained activity in this projection might be important to restrain risk seeking under the more ‘risky’ conditions.

In a different version of the lever-press task, head-fixed mice listened to a 5 s tone before the lever was presented; if the animal then pressed the lever, it had an 80% chance of receiving a reward and a 20% chance of being shocked. Computational analysis of the calcium responses of mPFC→NAc neurons showed that individual neurons could be classified as encoding the lever press, the reward or the footshock (with the largest fraction of cells encoding the shock). Furthermore, based on their activity during the initial 5 s tone, a subset of mPFC→NAc neurons predicted, with ~80% accuracy, whether the animal would press the lever or not. Interestingly, the activity of shock-encoding mPFC→NAc neurons during the 5 s tone was higher in ‘missed’ trials (that is, when the animal chose not to press) than in trials where the animal pressed the lever, whereas the activity of reward-encoding mPFC→NAc neurons did not predict any particular outcome. In other words, the activity of a subset of mPFC→NAc neurons that encode aversive shock could predict whether the animal sought a reward by pressing the lever.

To determine whether the activity of this subset of cells caused the suppression of lever pressing, the authors used a novel, dual-virus technique to enable targeted expression of a light-activated channel specifically in mPFC neurons that were activated by footshock. Strikingly, light stimulation of shock-responsive mPFC→NAc neurons (but not stimulation of all mPFC→NAc neurons) during the 5 s tone suppressed lever pressing.

Together, these findings show that, in mice, an increase in the activity of a subset of mPFC→NAc neurons that encode an aversive stimulus reduces risky reward seeking. The authors suggest that this top-down control mechanism may be relevant to disorders in which reward-seeking behaviour is affected, such as depression and addiction.

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